No Effect of Soy on Breast Proliferation in Small Study

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Consumption of soy isoflavones by postmenopausal breast cancer survivors doesn't appear to stimulate epithelial proliferative activity in the contralateral breast, according to a small pilot study.

This is a reassuring, albeit still preliminary, observation. The great majority of breast cancer patients are postmenopausal. They are discouraged from using hormone therapy to manage their menopausal symptoms, which can be quite severe. Soy supplements, which are rich in phytoestrogens, are growing in popularity as a nonpharmacologic alternative, Melanie R. Palomares, M.D., noted at a breast cancer symposium sponsored by the Cancer Therapy and Research Center.

Because preclinical work had shown conflicting stimulatory and inhibitory effects of soy isoflavones on breast tissue, Dr. Palomares and her coinvestigators launched the University of Washington/Seattle Cancer Care Alliance Phytoestrogen Trial. Participants were randomized to 100 mg/day of isoflavone tablets or placebo. Ultrasound-guided core biopsies of the contralateral breast were taken at baseline and after 6 and 12 months of therapy, explained Dr. Palomares of City of Hope National Medical Center in Duarte, Calif.

She reported on 23 postmenopausal disease-free women previously diagnosed with and treated for in situ or early-stage invasive breast cancer who have completed the year-long randomized trial.

The primary study end point was change in Ki-67 index, a widely used measure of epithelial proliferation. Ki-67 levels were elevated in both treatment and control groups at baseline, which was to be expected in light of the known elevated risk of contralateral breast cancer in women with a history of breast cancer. The Ki-67 index dropped steadily throughout the 12 months of follow-up, indicative of a decline in breast epithelial proliferation. The decline was greater in soy isoflavone–treated women, although not significantly so.

Hyperplasia was present in the contralateral breast tissue samples of 10 patients at baseline and 5 patients after a year. The treatment groups were too small to show significant differences in serial histology. There was a trend toward decreased estrogen receptor expression over time in both the soy isoflavone– and placebo-treated groups, but no significant differences between the two study arms. ■

Night Sweats More Common in Women With Infertility History

BY KATE JOHNSON
Montreal Bureau

PHILADELPHIA — Women with a self-reported history of infertility are more likely than fertile women to experience night sweats when they reach the perimenopause, according to Brandon J. Bankowski, M.D.

"This is a unique observation," he said at the annual meeting of the American Society for Reproductive Medicine.

"Women who experience these menopausal symptoms may have had something going on throughout their lives that manifested itself as infertility earlier on and then as night sweats later," he told this newspaper.

Dr. Bankowski and his associates recruited 435 women between 45 and 54 years of age with an intact uterus, ovaries, and at least three menstrual periods in the last year. The women provided one blood sample for the measurement of their estradiol (E2) and estrone (E1) levels. They also completed an extensive questionnaire regarding personal demographics; parity; and reproductive history, including a specific question about their self-reported history of an inability to conceive within 1 year of trying.

Slightly more than one-quarter of the women (27%) reported a history of infertility, and these women had no other significant differences in baseline characteristics, compared with controls.

When study participants were asked about 10 different menopausal symptoms, the only significant difference between the women with infertility cases and controls was in their reporting of night sweats, said Dr. Bankowski, a fellow in reproductive medicine at Johns Hopkins University, Baltimore.

Infertile patients were more likely to report night sweats in every frequency category. For example, 26% of the infertile women reported one episode of night sweats per night, compared with none of the controls. Almost 14% of the infertile women reported two episodes per night, compared with 4% of controls. Almost 5% of infertile women but none of the controls indicated they had more than four episodes per night. Blood tests on all the women revealed no differences in hormonal levels between the cases and controls.

"It's possible there's a common underlying mechanism that's creating both the infertility and the night sweats. This is important with regard to prevention and treatment," he said.

Dr. Bankowski said they hope next to follow infertile patients prospectively to see if they develop more night sweats than fertile controls. ■

Investigational DMPA-SC Treats Endometriosis Pain, Curbs BMD Loss

BY ROBERT FINN
San Francisco Bureau

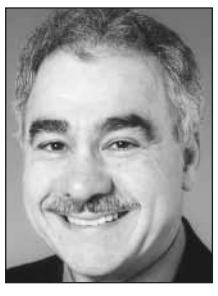
SAN FRANCISCO — An investigational form of depot medroxyprogesterone acetate is as effective as leuprolide for the treatment of endometriosis-associated pelvic pain, but it's significantly safer and better tolerated, Anthony A. Luciano, M.D., said at the annual meeting of the American Association of Gynecologic Laparoscopists.

The new formulation, called DMPA-SC (depot medroxyprogesterone acetate–subcutaneous), resulted in significantly smaller losses in bone mineral density (BMD) and significantly fewer menopausal symptoms than did leuprolide in the prospective, randomized, investigator-blinded study, said Dr. Luciano of the University of Connecticut in Farmington.

DMPA-SC has not been approved by the Food and Drug Administration. The study was funded by its manufacturer, Pharmacia Upjohn, a company that has become part of Pfizer Inc. Dr. Luciano acknowledged receiving consulting and honorarium support from Pfizer.

During the study, 274 women aged 18-49 years who had diagnoses of endometriosis-associated pelvic pain received 6 months of treatment with either DMPA-SC (104 mg every 3 months) or leuprolide (11.25 mg IM every 3 months). They were followed for an additional 12 months after completing treatment.

Patients rated their pain in five categories: dysmenorrhea, dyspareunia, pelvic pain, pelvic tenderness, and induration. Investigators used the Kupperman Index—a composite score involving 11 menopausal symptoms—to assess hypoestrogenemia.



The new formulation resulted in fewer menopausal symptoms than did leuprolide.

DR. LUCIANO

Both groups experienced substantial improvements in their pelvic pain, both at the end of treatment and continuing 12 months later, with no significant differences between the two groups.

Both groups showed some BMD declines at the end of treatment, but the mean losses were significantly less for women taking DMPA-SC than for women taking leuprolide in both the femur (0.3% vs. 1.65%) and the spine (1.1% vs. 3.95%).

Those who'd been taking DMPA-SC saw their BMD return to pretreatment levels 12 months after discontinuing treatment, whereas those who had been taking leuprolide showed continued BMD losses: 1.3% in the femur and 1.7% in the spine.

Women taking leuprolide had significant increases in Kupperman Index scores; those taking DMPA-SC showed no increase. Between the second and sixth month of treatment, women taking leuprolide experienced an average of two to three hot flashes per day. Women on DMPA-SC had almost no hot flashes. A significantly higher percentage of leuprolide patients had estradiol levels lower than 41 pg/mL (77% vs. 33%).

Adverse events seen more often in the DMPA-SC group were injection-site reactions (6.9% vs. 0%) and intermenstrual bleeding (5.4% vs 0.7%). ■

OC May Protect Against The Development of Rheumatoid Factor

BY TIMOTHY F. KIRN
Sacramento Bureau

SAN ANTONIO — Oral contraceptive use appears to be inversely associated with being rheumatoid-factor positive, Kevin D. Deane, M.D., said in a poster presentation at the annual meeting of the American College of Rheumatology.

In his study, 90% of 256 women had used an oral contraceptive at some time and 10% were positive for rheumatoid factor. The odds ratio of a woman being positive for rheumatoid factor was 0.18 if she had used oral contraceptives.

The women were mothers of children selected as part of an investigation into the heritability of type 1 diabetes. They were chosen for the study because of the likelihood of their having the HLA-DR4 allele, which is associated with both diabetes and rheumatoid arthritis.

Among the other factors examined were breast-feeding; use of nicotine, coffee, and injectable hormones; and age. None of these factors had as strong an association—either positively or negatively—as the use of oral contraception, said Dr. Deane of the University of Colorado, Denver.

The results "are significant statistically," Dr. Keane said in an interview.

He noted that higher endogenous estrogen levels have been shown to correlate somewhat with a lower incidence of rheumatoid arthritis, and that a decrease in those levels could predispose a woman to vulnerability.

Although Dr. Deane admitted that his findings are merely an intriguing observation, he added that if patients have another reason to take an OC, it's not unreasonable to tell them about the potential for arthritis prevention as an added benefit. ■

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